Clinical Policy: Ranibizumab (Byooviz, Cimerli, Lucentis, Susvimo)

Reference Number: CP.PHAR.186
Effective Date: 03.01.16
Last Review Date: 02.25
Line of Business: Commercial, HIM, Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Ranibizumab (Lucentis®, Susvimo®), ranibizumab-nuna (Byooviz®), and ranibizumab-eqrn (Cimerli™) are vascular endothelial growth factor (VEGF) inhibitors.

FDA Approved Indication(s)

Indication	Lucentis	Cimerli	Byooviz	Susvimo
Neovascular (wet) age-related macular degeneration (nAMD)	X	X	X	X (who have previously responded to at least two intravitreal injections of a VEGF inhibitor medication)
Macular edema following retinal vein occlusion (RVO)	X	X	X	-
Myopic choroidal neovascularization (mCNV)	X	X	X	-
Diabetic macular edema (DME)	X	X	-	X (who have previously responded to at least two intravitreal injections of a VEGF inhibitor medication)
Diabetic retinopathy (DR)	X	X	-	X (who have previously responded to at least two intravitreal injections of a VEGF inhibitor medication)

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Byooviz, Cimerli, Lucentis, and Susvimo are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Ophthalmic Disease Other Than Diabetic Macular Edema and Diabetic Retinopathy (must meet all)**:**

1. Diagnosis of one of the following (a, b, or c):*

**For DME and DR see section I.B. below*
   a. nAMD;
   b. Macular edema following RVO;
   c. mCNV;
2. Prescribed by or in consultation with an ophthalmologist;
3. Age ≥ 18 years;
4. Failure of bevacizumab intravitreal solution, unless contraindicated or clinically significant adverse effects are experienced;
   **Prior authorization may be required for bevacizumab intravitreal solution. Requests for IV formulations of Avastin, Mvasi, and Zirabev will not be approved*
5. If request is for Susvimo, member meets both of the following (a and b):
   a. Member has previously responded to at least 2 intravitreal injections of a VEGF inhibitor (e.g., intravitreal bevazicumab);
   b. Request is for the treatment of nAMD;
6. Dose does not exceed one of the following (a or b):
   a. For RVO or mCNV: 0.5 mg (1 vial/syringe) per month;
   b. For nAMD, either i or ii:
      i. If request is for Byooviz, Cimerli, or Lucentis: 0.5 mg (1 vial/syringe) per month;
      ii. If request is for Susvimo: 2 mg (one 100 mg/mL vial) per 6 months.

Approval duration:
mCNV: 3 months
All other indications: 6 months

B. Diabetic Macular Edema, Diabetic Retinopathy (must meet all)**:**
1. Request is for Cimerli, Lucentis, or Susvimo;
2. Diagnosis of one of the following (a or b):
   a. DME;
   b. DR;
3. Prescribed by or in consultation with an ophthalmologist;
4. Age ≥ 18 years;
5. Failure of bevacizumab intravitreal solution, unless contraindicated or clinically significant adverse effects are experienced;
   **Prior authorization may be required for bevacizumab intravitreal solution. Requests for IV formulations of Avastin, Mvasi, and Zirabev will not be approved*
6. If request is for Susvimo, member has previously responded to at least 2 intravitreal injections of a VEGF inhibitor (e.g., intravitreal bevazicumab);
7. Dose does not exceed one of the following (a or b):
   a. For DME, either i or ii:
      i. If request is for Cimerli or Lucentis: 0.3 mg (1 vial/syringe) per month;
      ii. If request is for Susvimo: 2 mg (one 100 mg/mL vial) per 6 months;
   b. For DR, either i or ii:
      i. If request is for Cimerli or Lucentis: 0.3 mg (1 vial/syringe) per month;
      ii. If request is for Susvimo: 2 mg (one 100 mg/mL vial) per 9 months.

Approval duration: 6 months

C. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**
1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
2. Member is responding positively to therapy as evidenced by one of the following (a, b, c, or d):
   a. Detained neovascularization;
   b. Improvement in visual acuity;
   c. Maintenance of corrected visual acuity from prior treatment;
   d. Supportive findings from optical coherence tomography or fluorescein angiography;
3. If request is for a dose increase, new dose does not exceed one of the following (a, b, c, or d):
   a. For DME, either i or ii:
      i. If request is for Cimerli or Lucentis: 0.3 (1 vial/syringe) mg per month;
      ii. If request is for Susvimo: 100 mg (1 vial) per 6 months;
   b. For DR, either i or ii:
      i. If request is for Cimerli or Lucentis: 0.3 (1 vial/syringe) mg per month;
      ii. If request is for Susvimo: 100 mg (1 vial) per 9 months;
   c. For RVO or mCNV: 0.5 mg (1 vial/syringe) per month;
   d. For nAMD, either i or ii:
      i. If request is for Byooviz, Cimerli, or Lucentis: 0.5 mg (1 vial/syringe) per month;
      ii. If request is for Susvimo: 2 mg (one 100 mg/mL vial) per 6 months.

Approval duration:
mCNV: 3 months
All other indications: 6 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid, or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

DME: diabetic macular edema
DR: diabetic retinopathy
FDA: Food and Drug Administration
mCNV: myopic choroidal neovascularization
nAMD: neovascular (wet) age-related macular degeneration
RVO: retinal vein occlusion
VEGF: vascular endothelial growth factor

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
bevacizumab (Avastin®)	**Neovascular (wet) AMD†:** 1.25 mg administered by intravitreal injection every 4 weeks	1.25 mg/month
	Macular edema secondary to RVO†:	1.25 mg/month

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	1.25 mg administered by intravitreal injection every 4 weeks	
	DR†: 1.25 mg administered by intravitreal injection every 6 weeks	1.25 mg/6 weeks
	DME†: 1.25 to 1.5 mg administered by intravitreal injection every 4 weeks	1.5 mg/month
	mCNV†: 1.25 mg initial intravitreal injection, followed by monthly evaluation for additional injections as needed	1.25 mg/month

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.
†Off-label

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Byooviz, Cimerli, Lucentis, Susvimo: ocular or periocular infections; hypersensitivity
  - Susvimo: active intraocular inflammation
- Boxed warning(s):
  - Byooviz, Cimerli, Lucentis: none reported
  - Susvimo: associated with a 3-fold higher rate of endophthalmitis than monthly intravitreal injections of ranibizumab

Appendix D: General Information

- In the Comparison of AMD Treatments Trials study, the difference in mean visual acuity improvement for patients treated with Avastin compared to Lucentis was -1.4 letters (95% [CI],- 3.7 to 0.8) at two years. The proportion of patients with arteriothrombotic events was similar in the Lucentis-treated patients (4.7%) compared to the Avastin-treated patients (5.0%; p=0.89). The proportion of patients with one or more systemic serious adverse events was higher with Avastin (39.9%) than Lucentis (31.7%; adjusted risk ratio, 1.30; 95% CI, 1.07-1.57; p = 0.009). Serious systemic adverse events included all-cause mortality, non-fatal stroke, non-fatal myocardial infarction, vascular death, venous thrombotic events, and hypertension.
- In the ANti-VEGF Antibody for the Treatment of Predominantly Classic CHORoidal Neovascularisation in AMD (ANCHOR) trial, the number of patients that lost fewer than 15 letters at 12 months was achieved by 96.4% of patients treated with Lucentis 0.5 mg compared to 64.3% of patients treated with Visudyne ($p < 0.001$). Rate of intraocular inflammation was higher for patients treated with Lucentis 0.5 mg at 15% compared to Visudyne at 2.8%.
- In the VEGF Trap-Eye: Investigation of Efficacy and Safety in Wet Age-Related Macular Degeneration (VIEW)-1 trial, the difference in the number of patients who lost fewer than 15 letters at 52 weeks between Eylea every 8 weeks compared to Lucentis was 0.6%

(95.1% CI -0.32, 4.4). In terms of the number of patients who gained at least 15 letters, the mean difference between Eylea every 8 weeks was 6.6% (95.1% CI -1.0, 14.1). There were no adverse events that were found to be significant from the Lucentis arm.

- In a trial comparing Eylea, Avastin and Lucentis, the Diabetic Retinopathy Clinical Research Network found in patients with diabetic macular edema that when the initial visual-acuity letter score was 78 to 69 (equivalent to approximately 20/32 to 20/40) (51% of participants), the mean improvement was 8.0 with Eylea, 7.5 with Avastin, and 8.3 with Lucentis ($p > 0.50$ for each pair wise comparison). When the initial letter score was less than 69 (approximately 20/50 or worse), the mean improvement was 18.9 with Eylea, 11.8 with Avastin, and 14.2 with Lucentis ($p < 0.001$ for Eylea vs. Avastin, $p = 0.003$ for Eylea vs. Lucentis, and $p = 0.21$ for Lucentis vs. Avastin).

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Ranibizumab (Lucentis), ranibizumab-nuna (Byooviz), ranibizumab-eqrn (Cimerli)	nAMD	0.5 mg (0.05 mL) administered by intravitreal injection once a month. <u>Alternative dosing:</u> Once monthly injections for three months followed by 4-5 doses dispersed among the following 9 months; or treatment may be reduced to one injection every 3 months after the first four injections if monthly injections are not feasible.	0.5 mg/month
	Macular edema following RVO	0.5 mg (0.05 mL) administered by intravitreal injection once a month.	0.5 mg/month
	mCNV	0.5 mg (0.05 mL) administered by intravitreal injection once a month for up to 3 months. Patients may be retreated if needed.	0.5 mg/month
Ranibizumab (Lucentis), Ranibizumab-eqrn (Cimerli)	DME and DR with or without DME	0.3 mg (0.05 mL) administered by intravitreal injection once a month	0.3 mg/month
Ranibizumab (Susvimo)	nAMD and DME	2 mg (0.02 mL of 100 mg/mL solution) continuously delivered via the Susvimo implant with refills every 24 weeks (approximately 6 months)	2 mg/6 months
	DR	2 mg (0.02 mL of 100 mg/mL solution) continuously delivered via the Susvimo implant with refills every 36 weeks (approximately 9 months)	2 mg/9 months

VI. Product Availability

Drug Name	Availability
Ranibizumab-nuna (Byooviz)	Single-dose glass vial: 0.5 mg/0.05 mL
Ranibizumab-eqrn (Cimerli)	Single-dose glass vials: 0.3 mg/0.05 mL, 0.5 mg/0.05 mL
Ranibizumab (Lucentis)	Single-use prefilled syringes: 0.3 mg/0.05 mL, 0.5 mg/0.05 mL
Ranibizumab (Susvimo)	Single-dose glass vial: 100 mg/mL

VII. References

1. Lucentis Prescribing Information. South San Francisco, CA: Genentech, Inc.; February 2024. Available at: https://www.lucentis.com/. Accessed November 15, 2024.
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3. Susvimo Prescribing Information. South San Francisco, CA: Genentech, Inc.; May 2025. Available at: https://www.susvimo.com/Accessed May 28, 2025.
4. Cimerli Prescribing Information. Redwood City, CA: Coherus BioSciences, Inc.; May 2024. Available at: https://www.cimerli.com. Accessed November 15, 2024.
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11. Wells JA, Glassman AR, Ayala AR, et al. Aflibercept, bevacizumab, or ranibizumab for diabetic macular edema. *N Engl J Med*. 2015 Mar 26;372(13):1193-203. doi: 10.1056/NEJMoa1414264.

12. Cheung C, Arnold JJ, Holz FG, et al. American Academy of Ophthalmology: Myopic choroidal neovascularization: review, guidance, and consensus statement on management. *Ophthalmology*. 2017 Nov; 124:1690:1711. http://dx.doi.org/10.1016/j.ophtha.2017.04.028

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J2778	Injection, ranibizumab, 0.1 mg
J2779	Injection, ranibizumab, via intravitreal implant (susvimo), 0.1 mg
Q5124	Injection, ranibizumab-nuna, biosimilar, (byooviz), 0.1 mg
Q5128	Injection, ranibizumab-eqrn, biosimilar (cimerli), 0.1 mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q 2021 annual review: no significant changes; references to HIM.PHAR.21 revised to HIM.PA.154; references reviwed and updated.	12.01.20	02.21
Ad Hoc update: updated redirection to "bevacizumab intravitreal solution" given availability of generic bevacizumab intravitreal solution and considering goal was to minimize use of IV bevacizumab products, most notably biosimilars; converted redirection language to "must use"	03.04.21	
Ad Hoc update: converted redirection language from "must use" to "Failure of" bevacizumab intravitreal solution.	08.03.21	
1Q 2022 annual review: no significant changes; added legacy WCG line of business (WCG.CP.PHAR.186 to be retired); for legacy WCG: removed redirection to Mvasi for DME, shortened approval durations from 12 months to 3 months for mCNV and 6 months for all other indications; RT4: added Byoorivz and Susvimo to policy; references reviewed and updated.	11.09.21	02.22
Spelling corrected for "refill" in Section V and "glass" in Section VI.	04.28.22	
Added HCPCS code for Byooviz [Q5124].	07.26.22	
RT4: added Cimerli to policy; added HCPCS code for Susvimo [J2779]. Template changes applied to other diagnoses/indications and continued therapy section.	08.23.22	
1Q 2023 annual review: no significant changes; references reviewed and updated.	11.17.22	02.23
Added HCPCS code for Cimerli [Q5128].	04.17.23	
1Q 2024 annual review: no significant changes; references reviewed and updated.	11.02.23	02.24

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Ad hoc: in intial approval criteria, separated DME and DR into a new section and clarified request is for Cimerli or Lucentis.	08.21.24	
1Q 2025 annual review: simplified FDA approved indications to show Lucentis and Cimerli are additionally indicated from Byooviz for DME and DR; added quantity limit of 1 vial/syringe for Lucentis and biosimilars; revised Susvimo maximum dose to 100 mg (1 vial) per 6 months per PI; in Appendix B per Clinical Pharmacology, removed dosing for neovascular glaucoma, updated dosing regimens, clarified off-label indications; removed Lucentis single-use glass vials in Section VI per PI, references reviewed and updated.	11.15.24	02.25
RT4: for Susvimo, updated FDA indication to include DME and clarified maximum dose is 2 mg (one 100 mg/mL vial) per 6 months.	02.12.25	
RT4: for Susvimo, updated FDA indication to include DR.	05.28.25	

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.